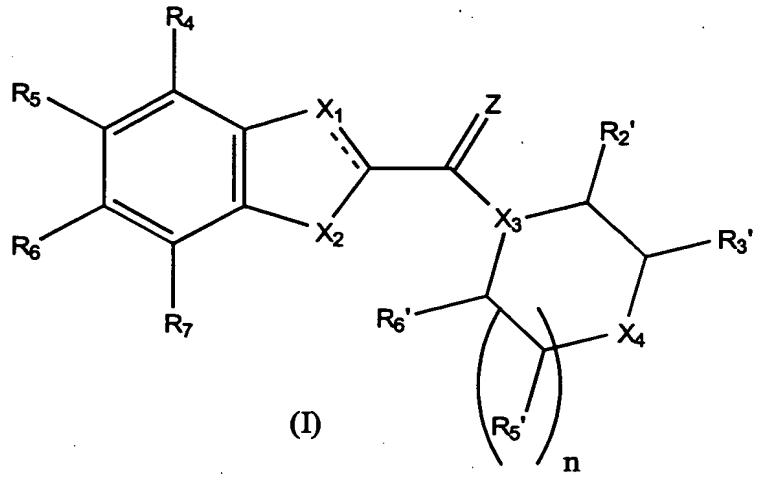
What is claimed is:

Claims

1. A method for treating allergic rhinitis in a patient, said method comprising administering to the patient a pharmaceutically effective amount of a composition comprising a compound of formula (I):



(I)

Wherein R_1 is R_a, R_aR_b-, R_a-O-R_b-, or $(R_c)(R_d)N$-R_b-, where R_a is H, cyano, -(C=O)N(R_c)(R_d), -C(=NH)(NH_2), C $_{1-10}$ alkyl, C $_{3-8}$ alkenyl, C $_{3-8}$ cycloalkyl, C $_{2-5}$ heterocyclic radical, or phenyl; where R_b is C $_{1-8}$ alkylene, C $_{2-8}$ alkenylene, C $_{3-8}$ cycloalkylene, bivalent C $_{3-8}$ heterocyclic radical, or phenylene; and R_c and R_d are each independently H, C $_{1-8}$ alkyl, C $_{2-8}$ alkenyl, C $_{3-8}$ cycloalkyl, or phenyl;

$R_{2'}$ is H, methyl, ethyl, NR_pR_q, -(CO)NR_pR_q, -(CO)OR_r , -$CH_2NR_pR_q$, or CH_2OR_r; where R_p, R_q, and R_r are independently selected from C $_{1-6}$ alkyl, C $_{3-6}$ cycloalkyl, phenyl; (C $_{3-6}$ cycloalkyl)(C $_{1-2}$ alkylene), benzyl or phenethyl; or R_p and R_q taken together with the nitrogen to which they are attached, form a 4-7 membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, and N;

$R_{3'}$ is H, methyl, ethyl, NR_sR_t, -(CO)NR_sR_t, -(CO)OR_u , -$CH_2NR_sR_t$, or CH_2OR_u; where R_s, R_t, and R_u are independently selected from C $_{1-6}$ alkyl, C $_{3-6}$ cycloalkyl, phenyl; (C $_{3-6}$ cycloalkyl)(C $_{1-2}$ alkylene), benzyl or phenethyl; or R_s and R_t taken together with the nitrogen to which they are attached, form a 4-7

membered heterocyclic ring with 0 or 1 additional heteroatoms selected from O, S, and N;

$R_{5'}$ is methyl, ethyl, or H;

$R_{6'}$ is methyl, ethyl, or H;

$R_{7'}$ is methyl, ethyl, or H;

X_4 is NR_1 or S;

X_1 is CR_3;

R_3 is F, Cl, Br, CHO, R_f, R_fR_g-, R_f-O-R_g-, or $(R_h)(R_i)$N-R_g-, where R_f is H, C $_{1-6}$ alkyl, C $_{2-6}$ alkenyl, C $_{3-6}$ cycloalkyl, C $_{2-5}$ heterocyclic radical, or phenyl; where R_g is C $_{1-6}$ alkylene, C $_{2-6}$ alkenylene, C $_{3-6}$ cycloalkylene, bivalent C $_{3-6}$ heterocyclic radical, or phenylene; and R_h and R_i are each independently H, C $_{1-6}$ alkyl, C $_{2-6}$ alkenyl, C $_{3-6}$ cycloalkyl, or phenyl;

X_2 is NR_e or O; R_e is H or C $_{1-6}$ alkyl;

X_3 is N;

Z is =O or =S;

each of R_4 and R_6 is independently H, F, Cl, Br, I, COOH, OH, nitro, amino, cyano, C $_{1-4}$ alkoxy, or C $_{1-4}$ alkyl;

R_5 is H, F, Cl, Br, I, (C=O)R_j, OH, nitro, NR_jR_k, cyano, phenyl, -OCH_2-Ph, C $_{1-4}$ alkoxy, or C $_{1-4}$ alkyl;

R_7 is H, F, Cl, Br, I, (C=O)R_m, OH, nitro, NR_lR_m, cyano, phenyl, -OCH_2-Ph C $_{1-4}$ alkoxy, or C $_{1-4}$ alkyl;

wherein each of R_j, R_k, R_l, and R_m is independently selected from H, C_{1-6} alkyl, hydroxy, phenyl, benzyl, phenethyl, and C_{1-6} alkoxy;

each of the above hydrocarbyl (including alkyl, alkoxy, phenyl, benzyl, cycloalkyl, and so on) or heterocyclic groups being independently and optionally substituted with between 1 and 3 substituents selected from C $_{1-3}$ alkyl, halo, hydroxy, amino, and C $_{1-3}$ alkoxy;

wherein n is 0, 1, or 2; where n is 2, the moiety –$(CHR_{5'})_{n=2}$- is –($CHR_{5'}$-$CHR_{7'}$)- where $CHR_{5'}$ is between $CHR_{6'}$ and $CHR_{7'}$;

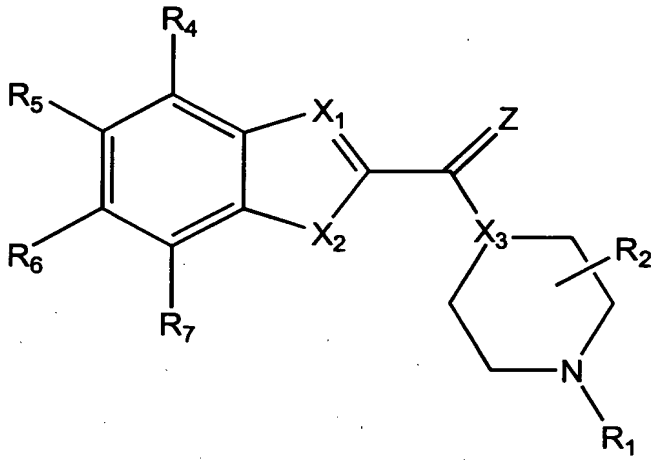
provided at least one of R_1, $R_{2'}$, R_3, R_4, R_5, R_6, and R_7 is other than H when Z is O;

and provided, where Z is O, n =1, and each of R_4, R_5, R_6, R_7, $R_{2'}$, $R_{3'}$, $R_{5'}$, and $R_{6'}$ is H, then (a) where X_2 is NH, then R_1 is (i) not methyl, pyridyl, phenyl, or benzyl, and (b) where X_2 is O, then R_1 is not methyl;

and provided, where Z is O, X_2 is NH, n = 1, R_1 is methyl, each of R_4, R_6, R_7, $R_{2'}$, $R_{3'}$, $R_{5'}$, and $R_{6'}$ is H, then R_5 is not methoxy;

or a pharmaceutically acceptable salt, ester, or amide thereof.

2. The method of claim 1 wherein said composition comprises a compound of the formula:



Wherein R_1 is R_a, R_aR_b-, R_a-O-R_b-, or $(R_c)(R_d)$N-R_b-, where R_a is H, C $_{1-10}$ alkyl, C $_{3-8}$ alkenyl, C $_{3-8}$ cycloalkyl, C $_{2-5}$ heterocyclic radical, or phenyl; where R_b is C $_{1-8}$ alkylene, C $_{3-8}$ alkenylene, C $_{3-8}$ cycloalkylene, bivalent C $_{3-8}$ heterocyclic radical, or phenylene; and R_c and R_d are each independently H, C $_{1-8}$ alkyl, C $_{2-8}$ alkenyl, C $_{3-8}$ cycloalkyl, or phenyl;

R_2 is ortho or meta, and is methyl or H;

X_1 is CR_3;

R_3 is F, Cl, Br, R_f, R_fR_g-, R_f-O-R_g-, or $(R_h)(R_i)$N-R_g-, where R_f is H, C $_{1-6}$ alkyl, C $_{2-6}$ alkenyl, C $_{3-6}$ cycloalkyl, C $_{2-5}$ heterocyclic radical, or phenyl; where R_g is C $_{1-6}$ alkylene, C $_{2-6}$ alkenylene, C $_{3-6}$ cycloalkylene, bivalent C $_{3-6}$ heterocyclic radical, or phenylene; and R_h and R_i are each independently H, C $_{1-6}$ alkyl, C $_{2-6}$ alkenyl, C $_{3-6}$ cycloalkyl, or phenyl;

X_2 is NR_e or O; R_e is H or C $_{1-6}$ alkyl;

X_3 is N;

Z is =O or =S;

each of R_4 and R_6 is independently H, F, Cl, Br, I, COOH, OH, nitro, amino, cyano, C_{1-4} alkoxy, or C_{1-4} alkyl;

R_5 is H, F, Cl, Br, I, $(C=O)R_j$, OH, nitro, NR_jR_k, cyano, $-OCH_2$-Ph, C_{1-4} alkoxy, or C_{1-4} alkyl;

R_7 is H, F, Cl, Br, I, $(C=O)R_m$, OH, nitro, NR_lR_m, cyano, C_{1-4} alkoxy, or C_{1-4} alkyl;

wherein each of R_j, R_k, R_l, and R_m is independently selected from H, C_{1-6} alkyl, hydroxy, phenyl, benzyl, phenethyl, and C_{1-6} alkoxy;

each of the above hydrocarbyl or heterocyclic groups being independently and optionally substituted with between 1 and 3 substituents selected from C_{1-3} alkyl, halo, hydroxy, amino, and C_{1-3} alkoxy;

provided at least one of R_1, R_2, R_3, R_4, R_5, R_6, and R_7 is other than H when Z is O;

or a pharmaceutically acceptable salt, ester, or amide thereof.

3. The method of claim 1 wherein said composition comprises a compound wherein R_1 is R_a, R_aR_b-, R_a-O-R_b-, or $(R_c)(R_d)N$-R_b-, where R_a is H, C_{1-10} alkyl, C_{2-5} alkenyl, C_{3-8} cycloalkyl, C_{2-5} heterocyclic radical, or phenyl; where R_b is C_{1-6} alkylene, or C_{2-8} alkenylene; and R_c and R_d are each independently H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{3-8} cycloalkyl, or phenyl;

$R_{2'}$ is methyl or H;

$R_{3'}$ is methyl or H;

$R_{5'}$ is methyl or H;

$R_{6'}$ is methyl or H;

$R_{7'}$ is methyl or H;

X_1 is CR_3;

R_3 is F, Cl, Br, methyl, ethyl, or propyl;

X_2 is NR_e or O; R_e is H or C_{1-6} alkyl;

X_3 is N;

Z is =O or =S;

each of R_4 and R_6 is independently H, F, Cl, Br, I, COOH, OH, nitro, amino, cyano, C $_{1-3}$ alkoxy, or C $_{1-3}$ alkyl;

R_5 is H, F, Cl, Br, I, $(C=O)R_j$, OH, nitro, NR_jR_k, cyano, $-OCH_2$-Ph, C $_{1-4}$ alkoxy, or C $_{1-4}$ alkyl;

R_7 is H, F, Cl, Br, I, $(C=O)R_m$, OH, nitro, NR_lR_m, cyano, C $_{1-4}$ alkoxy, or C $_{1-4}$ alkyl;

wherein each of R_j, R_k, R_l, and R_m is independently selected from H, C_{1-6} alkyl, hydroxy, phenyl, benzyl, phenethyl, and C_{1-6} alkoxy;

each of the above hydrocarbyl or heterocyclic groups being independently and optionally substituted with between 1 and 3 substituents selected from C $_{1-3}$ alkyl, halo, hydroxy, amino, and C $_{1-3}$ alkoxy;

n is 1;

provided at least one of R_1, $R_{2'}$, R_3, R_4, R_5, R_6, and R_7 is other than H when Z is O;

or a pharmaceutically acceptable salt, ester, or amide thereof.

4. The method of claim 1 wherein said composition comprises a compound wherein

R_1 is H, methyl, or ethyl;

One of $R_{2'}$ and $R_{3'}$ is methyl, and the other is H, where R_1 is H; R_2 is otherwise H;

X_1 is CR_3; R_3 is H, F, Cl, or Br;

X_2 is NR_e or O;

R_e is H or C $_{1-3}$ alkyl;

Z is =O or =S;

each of R_4 and R_6 is independently H, OH, C $_{1-4}$ alkyl, C $_{1-4}$ alkoxy, cyano, or amino;

R_5 is H, F, Cl, Br, COOH, OH, amino, cyano, C $_{1-4}$ alkoxy, or C $_{1-4}$ alkyl; and

R_7 is H, F, Cl, Br, C $_{1-4}$ alkyl, C $_{1-4}$ alkoxy, cyano, or amino;

provided at least one of R_5 and R_7 is not H.

5. The method of claim 1 wherein said composition comprises a compound wherein
R_1 is H, methyl, or ethyl;
$R_{2'}$ and $R_{3'}$ are independently methyl or H;
X_1 is CR_3 or N; R_3 is H, F, or Cl;
X_2 is NR_e or O; R_e is H or C_{1-6} alkyl;
Z is =O or =S;
each of R_4 and R_6 is H;
R_5 is H, F, Cl, Br, methyl, ethyl, or propyl; and
R_7 is H, F, Cl, Br, or C_{1-4} alkyl; provided at least one of R_5 and R_7 is not H.

6. The method of claim 1 wherein said composition comprises a compound wherein X_2 is N.

7. The method of claim 1 wherein said composition comprises a compound wherein X_2 is O.

8. The method of claim 1 wherein said composition comprises a compound wherein R_1 is H, methyl or ethyl.

9. The method of claim 1 wherein said composition comprises a compound wherein R_1 is methyl.

10. The method of claim 1 wherein said composition comprises a compound wherein $R_{2'}$ is H.

11. The method of claim 1 wherein said composition comprises a compound wherein $R_{2'}$ is methyl.

12. The method of claim 1 wherein said composition comprises a compound wherein R_3 is H or Cl.

13. The method of claim 12 wherein said composition comprises a compound wherein R_3 is Cl.

14. The method of claim 1 wherein said composition comprises a compound wherein R_5 is F, Cl, Br, or methyl and R_7 is F, Cl, or Br.

15. The method of claim 1 wherein said composition comprises a compound wherein each of R_5 and R_7 is independently selected from H, F, Cl, Br, and methyl, provided at least one of R_5 and R_7 is not H.

16. The method of claim 1 wherein said composition comprises a compound wherein each of R_4 and R_6 is independently H, methyl, or Cl.

17. The method of claim 1 wherein said composition comprises a compound wherein R_3 is H or Cl; R_5 is F, Cl, Br, or methyl; and R_7 is H, F, Cl, or Br.

18. The method of claim 17 wherein said composition comprises a compound wherein each of R_4 and R_6 is independently H, methyl, or Cl.

19. The method of claim 1 wherein said composition comprises a compound wherein Z is =S.

20. The method of claim 1 wherein said composition comprises a compound selected from: (5-Chloro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Fluoro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Bromo-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5,7-Difluoro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (7-Chloro-1H-indol-2-yl)-(4-methyl-

piperazin-1-yl)-methanone; (5,7-Dichloro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Chloro-7-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; and (3,5-Dichloro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone.

21. The method of claim 1 wherein said composition comprises a compound selected from: (6-Chloro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (1H-Indol-2-yl)-(3-methyl-piperazin-1-yl)-methanone; (7-Bromo-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Bromo-benzofuran-2-yl)-(4-methyl-piperazin-1-yl)-methanone; and (1H-Indol-2-yl)-(4-methyl-piperazin-1-yl)-methanethione.

22. The method of claim 1 wherein said composition comprises a compound selected from: (5-Chloro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Bromo-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5,7-Difluoro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; and (5,7- Dichloro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone.

23. The method of claim 1 wherein said composition comprises a compound selected from:

(4-Methyl-piperazin-1-yl)-(5-trifluoromethyl-1H-indol-2-yl)-methanone; (7-Amino-5-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Amino-7-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (7-Amino-5-bromo-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Amino-7-bromo-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Fluoro-7-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (7-Fluoro-5-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (6-Bromo-5-hydroxy-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-Bromo-6-hydroxy-1H-indol-2-yl)-(4-

methyl-piperazin-1-yl)-methanone; (6-Bromo-7-hydroxy-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (4-Bromo-7-hydroxy-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (6-Bromo-7-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; and (4-Bromo-7-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone.

24. The method of claim 1 wherein said composition comprises a compound selected from: (5,7-Dichloro-1H-indol-2-yl)-piperazin-1-yl-methanone; (5,7-Difluoro-1H-indol-2-yl)-piperazin-1-yl-methanone; (5,7-Difluoro-1H-indol-2-yl)-(3-methyl-piperazin-1-yl)-methanone; (5,6-Difluoro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone; and (4,6-Difluoro-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone.

25. The method of claim 1 wherein said composition comprises a compound selected from:
1-(5-Chloro-1H-indole-2-carbonyl)-4-methyl-piperazine-2-carboxylic acid methyl ester; 4-(5-Chloro-1H-indole-2-carbonyl)-1-methyl-piperazine-2-carboxylic acid methyl ester; 4-(5-Chloro-1H-indole-2-carbonyl)-1-methyl-piperazine-2-carboxylic acid amide; 1-(5-Chloro-1H-indole-2-carbonyl)-4-methyl-piperazine-2-carboxylic acid amide; 4-(5-Chloro-1H-indole-2-carbonyl)-1-methyl-piperazine-2-carboxylic acid methylamide; 1-(5-Chloro-1H-indole-2-carbonyl)-4-methyl-piperazine-2-carboxylic acid methylamide; 4-(5-Chloro-1H-indole-2-carbonyl)-1-methyl-piperazine-2-carboxylic acid dimethylamide; 1-(5-Chloro-1H-indole-2-carbonyl)-4-methyl-piperazine-2-carboxylic acid dimethylamide; (5-Chloro-1H-indol-2-yl)-(3-hydroxymethyl-4-methyl-piperazin-1-yl)-methanone; (5-Chloro-1H-indol-2-yl)-(3-methoxymethyl-4-methyl-piperazin-1-yl)-methanone; (5-Chloro-1H-indol-2-yl)-(2-methoxymethyl-4-methyl-piperazin-1-yl)-methanone; (5-Chloro-1H-indol-2-yl)-(4-methyl-3-

methylaminomethyl-piperazin-1-yl)-methanone; (5-Chloro-1H-indol-2-yl)-(4-methyl-2-methylaminomethyl-piperazin-1-yl)-methanone; (5-Chloro-1H-indol-2-yl)-(3-dimethylaminomethyl-4-methyl-piperazin-1-yl)-methanone; and (5-Chloro-1H-indol-2-yl)-(2-dimethylaminomethyl-4-methyl-piperazin-1-yl)-methanone.

26. The compound (5-Chloro-7-methyl-1H-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone.